REMARKS

Favorable consideration and allowance are respectfully requested for claims 1, 4, 8, 10, 13, 17, 18, and 25-29 in view of the foregoing amendments and the following remarks.

Claims 19-24 are cancelled without prejudice or any disclaimer of the subject matter therein.

The rejection of claims 1, 4, 8, 10, 13 and 17-29 under 35 U.S.C. § 112, first paragraph, as not being properly enabled, is respectfully traversed. The enablement requirement is satisfied where the specification describes the claimed subject matter in such a way as to enable any person skilled in the art to which it pertains to make and/or use the invention. Thus, enablement is judged in view of the combined teachings of the specification and the knowledge of one skilled in the art.

The present claims relate to compounds showing an affinity to nicotinic acetylcholine receptors and pharmaceutical compositions comprising an effective amount of these compounds for treating neurodegenerative diseases such as Alzheimer's disease or Parkinson's disease, dementia such as cerebrovascular dementia, motor ataxia such as Tourette's syndrome, neurosis during chronic cerebral infarction, neuropathy and mental disease such as anxiety and schizophrenia, as well as cerebral dysfunction caused by cerebral injury.

It is widely known that nicotine is highly useful in improving various cerebral functions such as increasing cerebral blood flow and increasing glucose uptake in the brain. It is also known that nicotine inhibits amyloid formation of β-peptides, which is believed to be a cause of neuronal cell death with Alzheimer's disease. Further, in patients suffering from Alzheimer's disease, the degeneration of acetylcholinergic neurons is affected and nicotinic acetylcholine receptors in the cerebral cortex and hippocampus are decreased. These

acetylcholinergic neurons are known to be one of the most important in the nervous system as they are responsible for cognition such as attention, learning, memory and recognition.

Thus, persons of skill in the art are aware of the relevance of nicotinic acetylcholine receptors in a wide variety of pharmaceutical applications and there have been many attempts to develop activators for $\alpha 4\beta 2$ nicotinic acetylcholine receptors in the central nervous system as medicines. See pages 1-7 of the present specification. In the present case, through extensive study of compounds which selectively bind $\alpha 4\beta 2$ nicotinic acetylcholine receptors of the central nervous system, the inventors of the present application discovered that the claimed compounds possess a high affinity to these nicotinic acetylcholine receptors and activate these receptors. Pages 12-17 of the specification detail methods of making these compounds so that a person of ordinary skill in the art would be able to make the claimed compounds. Suitable delivery forms for administration are described in the specification on pages 18 and 19. Suitable amounts of the compound to be administered are provided on page 19.

The U.S. Court of Customs and Patent Appeals has stated that "[t]he first paragraph of § 112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance." *In re Marzocchi*, 169 USPQ 367 , 369 (CCPA 1971). The court also added that "it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure." *In re Marzocchi*, 169 USPQ 367 , 370 (CCPA 1971).

The present record includes no such statement or other explanation as to why the truth of the accuracy of statements in the disclosure should be doubted.

Further, the specification includes ample evidence of a suitable use for the claimed compounds and the bioactivity of these compounds. Tables 15, 16 and 17, on pages 45-47 of the specification show the results of receptor binding studies of the compounds of the present invention. Table 18 on page 50 shows the results of agonist activity tests of various compounds of the present invention. This experimental data clearly shows that the claimed compound are relevant to and have an affinity for the $\alpha 4\beta 2$ nicotinic acetylcholine receptor.

A declaration from Dr. Yoshihiro Tani accompanies this reply and was previously provided to the U.S. Patent and Trademark Office in the application having serial no. 10/009,607. In his declaration, Dr. Tani details comparative research between ABT-418, (-)-nicotine, and compounds similar to those of the presently claimed invention. As noted on page 4 of the declaration, ABT-418 is a selective nicotinic agonist that caused significant improvement in learning and memory for human patients in the early stages of Alzheimer's disease. While ABT-418 is no longer being studied for other reasons, ABT-418 is a standard compound used for evaluating selective agonist activity at nicotinic acetylcholine receptor sites. Table 1 on page 4 of the declaration demonstrates the effectiveness of 6 representative compounds in producing nicotinic receptor activity and compares the activity of the compounds to that of ABT-418 and ( )-nicotine. The data in table 1 is based on an in vivo study of selective nicotinic receptor activity in mouse brains. At a minimum, the data in table 1 shows the comparable effectiveness of compounds similar to those presently claimed in treatment of Alzheimer's disease and for improving learning and memory. In relevant part, Dr. Tani declares:

> Clinical studies indicate that (-)-nicotine may be beneficial for treatment of impairment in attention and rapid information processing with Alzheimer's disease, and imply that not only the cholinergic system but also monoaminergic systems are possible mechanisms by which (-)-nicotine treatment improves cognitive performance. Among the monoaminergic systems, it has been

> suggested that noradrenergic effects of stimulants as important therapeutic mechanisms on enhancing capabilities such as attention and working memory.

Dr. Tani further declared that experimental results of *in vivo* assays on structurally similar compounds show that they affect norepinephrine (NE) turnover in the mouse whole brain, similar to the action of (-)-nicotine and ABT-418. The results in the declaration provide further support for the effectiveness of compounds similar to those presently claimed as nicotinic receptor agonists.

Thus, the specification as filed (i) specifically identifies the claimed compounds, (ii) provides a method of synthesizing these compounds and (iii) provides at least one use for the claimed compounds. As indicated above, the burden is on the Patent Office to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. On the present record there is no such explanation, and no apparent reason is offered to support the notion that the statements in the specification are not true or accurate.

As a result, the claims are properly enabled, and reconsideration and withdrawal of the rejection are respectfully requested.

The rejection of claims 1, 4, 8 and 19-29 under 35 U.S.C. § 112, first paragraph, as lacking adequate written description is respectfully traversed. To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail so that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003). An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and

formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

Claim 1 has been amended to delete the reference to nitro and cyano in the definition of R^8 and R^9 appearing in claim 1. As amended, this element of claim 1 is properly supported, for instance, by the specification on page 11, lines 24-30. Claims 4, 8, and 19-29 (to the extent the are still pending) depend from claim 1, either directly or indirectly. Accordingly, the claimed invention is shown in the specification and the written description requirement is satisfied. Reconsideration and withdrawal of this rejection are respectfully requested.

The rejection of claims 1, 4, 8, 10, 13 and 17-29 under 35 U.S.C. § 112, second paragraph, as indefinite, is respectfully traversed. Claim 18 has been made independent so that all of the terms therein have proper antecedent basis. Further, a period has been added to clarify the end of the claim.

The Examiner rejected claims 1, 4, 8, 10, 13 and 17-29 as indefinite for allegedly providing for the use of claimed compounds, but not setting forth steps to determine which disorders are capable of being treated by modulating acetylcholine receptor activity. Of the pending claims, only 8, 17 and 25-29 are directed to methods. Further, claims 25-29 all depend from claim 8 or 17 (directly or indirectly). Claims 8 and 17 are directed to methods of activating $\alpha4\beta2$ nicotinic acetylcholine receptors and do not recite treating, inhibiting or otherwise preventing any particular disease or disorder. Thus, these claims do not require treatment of any disease, much less any identification of what disease is being treated. Rather, the claims are directed to the physiological effect the compounds have on biological systems (activating $\alpha4\beta2$ nicotinic acetylcholine receptors). The claims do not recite, for instance, "treating a disease" without identifying that disease. Accordingly, for purposes of the definiteness of claims 8 and 17, it is irrelevant whether a given disease involves $\alpha4\beta2$ nicotinic acetylcholine receptor activity.

Rather, the relevant question is whether one of skill in the art could understand the scope of the claim. The MPEP states that:

> In reviewing a claim for compliance with 35 U.S.C. 112, second paragraph, the examiner must consider the claim as a whole to determine whether the claim apprises one of ordinary skill in the art of its scope and, therefore, serves the notice function required by 35 U.S.C. 112, second paragraph, by providing clear warning to others as to what constitutes infringement of the patent. See, e.g., Solomon v. Kimberly-Clark Corp., 216 F.3d 1372, 1379, 55 USPQ2d 1279, 1283 (Fed. Cir. 2000).

In the present case, that test is clearly met, because one of skill in the art would readily understand that the claims requires administering a claimed compound to activate $\alpha 4\beta 2$ nicotinic acetylcholine receptors. Therefore, one of skill in the art could readily determine whether or not some activity constitutes infringement of these claims.

Further, claims 25-29 specifically identify the relevant diseases. Thus, it cannot be true that further experimentation is required to determine which diseases respond to a treatment. The claims themselves inform one of skill in the art which diseases are relevant.

For all of the foregoing reasons, the claims are believed to be definite, and reconsideration and withdrawal of this rejection are respectfully requested.

The rejection of claims 1, 4, 10 and 18 under 35 U.S.C. § 102(b) as anticipated by EP 0 268 915 is respectfully traversed. Claim 1 is amended to delete the reference to pyridine and thizaole in the definition of A. The reference teaches thiazol and pyridine compounds. As amended, the claims do not include such compounds and the claimed compounds do not appear to be taught by the reference. Thus, the reference fails to disclose every element of the claimed invention. Reconsideration and withdrawal of the rejections are respectfully requested.

The rejection of claims 1, 4, 8 and 19-22 under 35 U.S.C. § 102(b) as anticipated by Chao is respectfully traversed. The Examiner alleges that compound number 4 on page 79 is relevant, however, this compound includes an NNO_2 group rather than an NH_n group as is required in claim 1. Claims 19-24 have been cancelled. None of the other compounds cited in the reference are believed to be relevant to the pending claims, as the claims do not include the disclosed compounds. Thus, the reference fails to disclose or suggest the compounds of the claimed invention. Accordingly, reconsideration and withdrawal of the rejections are respectfully requested.

The rejection of claim 1 under 35 U.S.C. § 102(b) as anticipated by any of Brown et al., Cox et al. and Janssens et al. is respectfully traversed. Claim 1 has been amended to delete the reference to "halogen", "nitro" and "cyano" in the definition of A, as well as "pyridine" and "thizaole" (as indicated above). Accordingly, the claims do not include compounds where: A is phenyl substituted by a nitro group (Brown et al.); A is 6-chloro-pyridin-3-yl (Cox et al.); or A is 4-fluorophenyl (Janssens et al.) Further, Brown does not appear to provide the methyl bridge which attaches the A group as claimed. Thus, the references fails to disclose or suggest the compounds of the claimed invention. Reconsideration and withdrawal of the rejections are respectfully requested.

CONCLUSION

In view of the foregoing, the application is respectfully submitted to be in condition for allowance, and prompt favorable action thereon is earnestly solicited.

If there are any questions regarding this amendment or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323 (Docket #100598.50325).

Respectfully submitted,

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